UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/978,217	11/25/97	BENZ	C 02307E-07111

HM12/0103

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EXAMINER	
HOLLERAN, A	
ART UNIT	**PAPER NUMBER**
1642	17

DATE MAILED: 01/03/01

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/978,217	Benz, C.C. et al.
Examiner	**Group Art Unit**
Ann Holl ran	1642

☒ Responsive to communication(s) filed on *Oct 2, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-14, 16-18, 20-26, 71, 79, 82, and 83* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-14, 16-18, 20-26, 71, 79, 82, and 83* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This Office Action is responsive to the Amendment filed October 2, 2000.

Claims 15, 19, 27-70, 72-78, 80 and 81 were canceled.

Claims 82 and 83 were added.

Claims 1-14, 16-18, 20-26, 71, 79, 82 and 83 are pending and examined on the merits. Claim 79 is examined to the extent that it reads on a kit for the detection of a ESX gene, said kit comprising a container containing an ESX nucleic acid or subsequence thereof.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

3. The rejection of claims 1-9 under 35 U.S.C. 112, first paragraph, because the specification does not enable the full scope of the claimed invention is withdrawn in view of the amendment of claims 1-9 and upon further consideration of the grounds of the rejection.

4. The rejection of claims 1-9 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession

of the claimed invention is withdrawn in view of the amendment of claims 1-9 and upon further consideration of the grounds of the rejection.

5. The rejection of claims 1, 2, 5, 7, 15, 16, 17 and 27 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn upon further consideration.

6. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Filloux et al (Filloux, A. et al, EMBO J., 9: 4323-4329, 1990) is withdrawn in view of the amendment of claim 1.

7. The rejection of claim 16 under 35 U.S.C. 102(b) as being anticipated by either Giovane et al (Giovane, A. et al, Genes Dev., 8: 1502-1513, 1994) or Dalton et al (Dalton, S. et al, 68: 597-612, 1992) is withdrawn in view of the amendment of claim 16.

8. The rejection of Claims 10-14 under 35 U.S.C. 103(a) as being unpatentable over either Accession No. R50578, Accession No. H12657, Accession No. T27397 or Accession No. R73021 in view of Promega Corporation (Promega Protocols and Applications Guide, Promega

Corporation, pages 145-153, 1991) is withdrawn in light of the amendment to claim 10 deleting the reference to a labeled nucleic acid.

Claim Rejections Maintained:

9. The rejection of claims 1-9, and 16-26 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained. The rejection of claims 15 and 27 is withdrawn in view of the amendment canceling these claims. The rejection is newly applied to claims 10-14, 82 and 83 because of the amendment to claim 1 from which claims 10-14, 82 and 83 depend. Thus, claims 1-14, 16-26, 82 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 16 are vague and indefinite because the claims are drawn to nucleic acids which specifically hybridize to a human ESX nucleic acid under stringent conditions (claims 1-14, 82 and 83) or specifically hybridize to a murine ESX nucleic acid under stringent conditions (claims 16-26). Applicant argues that the specification provides teachings which would enable one of skill in the art to assess the metes and bounds of claims 1 and 16. Applicant's arguments have been considered but not found persuasive. The passage of the specification pointed to by Applicant merely describes the many variables that affect hybridization between two nucleic acids but does not provide a specific set of conditions that would allow one of skill in the art to know

which structures fall within the scope of the claims and which do not. The difference between the example (Example 9) in the Interim Guidelines for Written Description and the instant case is that in the Interim Guidelines the phrase "highly stringent hybridization conditions" was interpreted to be a specific set of conditions (6XSSC and 65 degrees Celsius). No teachings in the specification or in Applicant's argument allows such a narrow interpretation of the phrase "stringent conditions" in claims 1 and 16.

10. The rejections of claims 1, 4-16, 19-27 and 71 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,789,200 (Kola et al, published Aug. 4, 1998; filed Nov. 15, 1996; effective U.S. filing date Oct. 31, 1996) is maintained. The rejection of claims 4, 15, 19 and 27 is withdrawn in upon further consideration (for claim 4) and in light of the amendment canceling claims 15, 19 and 27. The rejection is newly applied to claim 2. The rejection is applied to new claims 82 and 83. Thus, claims 1, 2, 5-14, 20-26, 82 and 83 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 5,789,200 for the reasons of record. With regard to claim 2, U.S. Patent 5,789,200 discloses a nucleotide sequence (SEQ ID NO: 1) which encodes a polypeptide comprising the sequence of SEQ ID NO: 2.

11. The rejection of Claim 79 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,789,200 is maintained for the reasons of record.

U.S. Patent 5,789,200 discloses that polynucleotides such as that of disclosed SEQ ID NO: 1 may be employed as research reagents in polynucleotide assays (column 13, lines 47-51 and column 23, line 1 column 25, line 58). Thus, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to have assembled the polynucleotides disclosed by U.S. Patent 5,789,200 into kits for purposes of increased marketability, convenience and reliability.

New Grounds of Rejection:

12. Claim 79 is objected to because it is drawn to multiple patentably distinct products as discussed in previous Office Actions (mailed 5/24/99 and 3/30/00). Applicant is required to amend claim 79 to delete references to the polypeptide and antibody products.

13. Claims 1-14, 16-18, 20-26, 71, 79, 82 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of "human ESX nucleic acid" to identify the target nucleic acid structure to which the claimed nucleic acids will hybridize. The specification does not define "human ESX nucleic acid" as a discrete nucleic acid structure.

Claim 14 is vague and indefinite because it lacks antecedent basis for "said label".

Claim 16 is vague and indefinite because "said murine ESX" lacks antecedent basis. This rejection would be obviated by amending "said murine ESX" to read "said murine ESX nucleic acid".

Claims 71 and 79 are vague and indefinite in the recitation of the terms "ESX transcription factor" or "ESX gene" or "ESX polynucleotide" because the specification does not reasonably apprise one of skill the art what structures are encompassed by these terms. The specification describes ESX genes and polypeptide as belonging to the ETS family of transcription factors because ESX genes and polypeptide have significant homology to other known ETS transcription factors. The term "significant homology" is not defined. The specification also describes ESX genes and polypeptide as distinct from other known ETS transcription factors because of the occurrence of five non-conservative substitutions in the ETS consensus sequence. The location and identity of the non-conservative substitutions is not described and the specification does not define whether the presence of the undefined non-conservative substitutions is a necessary feature of an ESX gene or polypeptide.

14. Claims 1, 4-14, 16, 20-26, 71, 79, 82 and 83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The basis for this rejection is that the specification provides inadequate description to support the claimed genus of polynucleotides.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art, as of the filing date sought, that he or she was in possession of the invention. The invention, for purposes of the 'written description' inquiry, is whatever is now claimed." (See page 1117). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Because the claimed nucleic acids vary considerably in structure and because nucleic acids products are used to make polypeptide products, it stands to reason that the claimed nucleic acids will encode polypeptide products which vary considerably in structure. It is well known that even small changes in the primary sequence of a protein can lead to large changes in protein function (see for example, Lazar, E. et al. Molecular and Cellular Biology, 8(3): 1247-1252, 1988 and

Burgess, W.H. et al. J. Cell Biology 111: 2129-2138, 1990) which leads to the highly unpredictable nature of protein chemistry. Without a reasonable ability to predict the function of the encoded protein products, the skilled artisan cannot envision the many protein products encoded by the claimed nucleotides. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation of the claimed nucleic acids. Adequate written description of a genus of nucleic acids requires more than a mere statement that the encompassed species are part of the invention. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

A. Rejection of claims 1, 4-6, 8, 9, 82 and 83

Claim 1 is construed to be drawn to any nucleic acid which hybridizes to a human ESX nucleic acid. Dependent claim 4 is limited to those species which are amplified from a genomic library using primer pairs designated by SEQ ID NO: 13 and SEQ ID NO: 14. Dependent claim 5 is limited to those nucleic acids which hybridize to SEQ ID NO: 1. The nucleic acids of dependent claim 6 further comprise a vector. Dependent claims 8 and 9 are limited to those nucleic acids which have a smallest sum probability of either 0.5 or 0.2 when compared to SEQ ID NO: 6 using a BLASTN algorithm. Dependent claims 82 and 83 add the limitation that the nucleic acids are labeled.

The specification discloses SEQ ID NO: 1 and the amino acid sequence of SEQ ID NO: 2 which provides for all of the species of nucleic acid which consist of a coding sequence for the

amino acid sequence of SEQ ID NO: 2. However, claim 1 encompasses species of nucleic acid which may be as small as one nucleotide. In addition, because the term "human ESX nucleic acid" is not defined structurally, the claim is drawn to nucleic acids which hybridize to an undefined target sequence. Furthermore, because the term "stringent conditions" is not defined in the claim, the extent of the variability between the hybridizing sequence and the complete complement of the target sequence cannot be determined. Thus, claim 1 encompasses a genus of nucleic acids which vary considerably in structure and function; and the structure of SEQ ID NO: 1 or the structures of all of the coding sequences for SEQ ID NO: 2 are not representative of the claimed genus.

The limitations provided by claims 4-6, 8, 9, 82 and 83 do not limit the claimed genus of nucleic acids to encompass species that are similar in structure and function to SEQ ID NO: 1 and SEQ ID NO: 2. In the case of claim 4, the amplification conditions are not provided which would limit the variability of the nucleic acid products derived from the amplification procedure. In the case of claim 5, although the structure of the target sequence is provided, the claimed nucleic acids vary considerably because the phrase "stringent conditions" allows for many nucleotide substitutions and because there is no size limitation. In the case of claims 6, 82 and 83, the limitations merely provide for the addition of a vector sequence or a label to the nucleic acids which are encompassed by claim 1. In the case of claims 8 and 9, the BLASTN comparison between SEQ ID NO: 6 (a partial sequence derived from SEQ ID NO: 1) does not limit the nucleic acids to only those species which have the same size as SEQ ID NO: 6; and even if it did,

the structure and function of the claimed nucleic acids would still vary considerably from the structure and function of the disclosed SEQ ID NO: 1 and SEQ ID NO: 2.

B. Rejection of claims 7 and 10-14

Claim 7 is construed to be drawn to nucleic acids comprising nucleic acids which encode the amino acid of SEQ ID NO: 7 which a sequence of part of the protein defined by SEQ ID NO: 2. Thus, claim 7 is drawn to nucleic acids comprising nucleic acids encoding a partial protein product. Claim 10 is construed to be drawn to nucleic acids comprising nucleic acids that encode the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence containing conservative substitutions of said amino acid sequence. SEQ ID NO: 12 is a sequence of part of the protein defined by SEQ ID NO: 2. Thus, claim 10 and dependent claims 11-14 are drawn to nucleic acids comprising nucleic acids encoding a partial protein product. Claims 11-14 add limitations that the claimed nucleic acids are free of dideoxynucleotides, that the nucleic acid is single stranded, that the nucleic acid is a sense strand and the nucleic acid is labeled with a radionuclide.

Because of the open language which allows the addition of nucleotides on either end of the described nucleic acids and because the claims are drawn to nucleic acids defined in structure as those species which encode partial proteins or those species which encode partial proteins containing conservative substitutions, the nucleic acids encompassed by claims 7 and 10-14 vary considerably in structure and function from the disclosed nucleic acid of SEQ ID NO: 1 or nucleic acids comprising a coding sequence for the polypeptide of SEQ ID NO: 2. Thus, the protein

products will vary considerably in structure and function which does not allow one of skill in the art to find that Applicant was in possession of the claimed genus of nucleic acids.

C. Rejection of claims 16 and 20-26

Claims 16 and 20 is construed to be drawn to any nucleic acid which hybridizes to the nucleic acid set forth in SEQ ID NO: 15. The nucleic acid set forth in SEQ ID NO: 15 is a genomic sequence which includes non-coding regions. The nucleic acids of dependent claim 21 further comprise a vector. Claims 22-26 add limitations that the claimed nucleic acids are labeled, and wherein the labeled nucleic acid is free of dideoxynucleotides, is single stranded, is a sense strand and that the label is a radionuclide.

The specification discloses SEQ ID NO: 15 and the amino acid sequence of SEQ ID NO: 16 which provides for all of the species of nucleic acid which consist of a coding sequence for the amino acid sequence of SEQ ID NO: 16. However, claim 16 encompasses species of nucleic acid which may be as small as one nucleotide. Because the term "stringent conditions" is not defined in the claim, the extent of the variability between the hybridizing sequence and the complete complement of the target sequence cannot be determined. Furthermore, because there is no size limitation or functional limitation, species encompassed by claim 16 are those that hybridize to non-coding regions and thus do not encode for any protein product. Thus, claim 16 and dependent claims 20-26 each encompass a genus of nucleic acids which vary considerably in structure and function; and the structure of SEQ ID NO: 15 or the structures of all of the coding sequences for SEQ ID NO: 16 are not representative of the claimed genus.

D. Rejection of claims 71 and 79

Claim 71 is drawn to a transfected cell comprising a heterologous gene encoding an ESX transcription factor. Claim 79 is construed to be drawn to a kit for the detection of a ESX gene, said kit comprising a container containing an ESX nucleic acid or subsequence thereof. For the purposes of examination, the terms "ESX transcription factor" and "ESX nucleic acid" are interpreted to encompass any of the nucleic acid species encompassed by claims 1 or 16. As outlined above, the disclosure of the specification does not provide an adequate written description of the genus of nucleic acids encompassed by either of claims 1 and 16. Therefore, the specification does not provide an adequate written description of the claimed cells or kits.

Conclusion

No claim is allowed. This rejection is not made final because of new grounds rejection.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
December 29, 2000

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